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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/801,751 | 03/09/2001 | Jean-Pierre Robin | 017751-021 | 5968 |

7590 02/12/2003

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| EXAMINER |
|---|
| GOLDBERG, JEROME D |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | |

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/801,751 | ROBIN ET AL. | |
| | Examiner | Art Unit | |
| | Jerome D Goldberg | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2,4-6,9,10,12-17,19-21,24 and 28-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4-6,9,10,12-17,19-21 and 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 23, 2003 has been entered.

Applicants elected the compounds of claim 2, i.e. harrengtonine and homoharringtonine with traverse in Paper No. 9. The instant claims are still being examined as they read on the above compounds.

Applicants are still required to reduce the scope of the instant claims to the elected invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 4-6, 9, 10, 12-17, 19-21 and 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Li et al. reference of record or the Takeda et al. reference of record taken with the Reg. No. H271 or the Whaun et al. reference (both presented by applicants in Paper No. 16). The Li et al reference teaches "injection (i.e.) of herringtonine (1) ... (26 mg/kg) and homoharringtonine (11)... (1 mg/kg) into L 1210 leukemia mice both produced apoptosis ... in leukemia cells "(AB, line 1-4).

The Takeda et al. reference teaches that the "HA and HO had significant activates against P388 leukemia, L1210 leukemia ... by i.p. injection" (AB, line 4-6) (The HA and HO are the elected compounds). The Reg. No. H 271 states in col. 3, line 41 to col. 4, line 2 that "pathologically. L1210 tumor cells in culture exposed to homoharringtonine demonstrated karyorrhexis of nuclear constituents. Similar morphological changes were seen on blood film of plasmodium folciparun infected red cell cultures exposed to homoharringtonine". The reference further states that "effective dosage for homoharringtonine given subcutaneously is 3-8 mg/kg per day.." (col. 4, line 41-42) and that "clinical cancer studies showed safe dosages of 5.0 mg/$m^2$ administered by continuous infusion" and that" and average man has a surface area of about 1.7 $m^2$, therefore clinical studies would indicate safe daily doses of 8.5 mg" (col. 5, lines 2-6 after Table 3).

The Whaun et al. reference states on the last three lines of page 229 that "we were interested in cephalotaxine esters, especially harringtonine and

homoharringtonine, because they are promising antitumor agents and have been found safe in human trials"... and on page 230, last three lines that "the brochure includes reports ... of Chinese clinical studies ... of the use of cephalotaxis alkaloid drugs for the treatment of leukemia. The dose of harringtonine used in the Chinese studies ranges ..."

The reference shows subcutaneous injections (see page 234, line 5). The reference fails to teach treating leukemia by subcutaneous injection. Accordingly, one skilled in this art would find ample motivation from the prior art supra to employ the well known anti-leukemia drugs harringtonine and homoharringtonine by subcutaneous injection with a reasonable expectation that said anti-leukemia drugs would be effective for treating leukemia drugs were administered in the prior art by subcutaneous administration to treat other conditions (see the Reg. No. H271 and the Whaun et al. reference).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerome Goldberg whose telephone number is (703) 308-4606. The examiner can normally be reached on Monday to Thursday from 9:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Goldberg/LR
February 11, 2003

JEROME D. GOLDBERG
PRIMARY EXAMINER